

AMENDMENT AND RESPONSE UNDER 37 CFR § 1.111

Serial Number: 09/801,221

Filing Date: 3/7/2001

Title: Human Cord Blood as a Source of Neural Tissue for Repair of the Brain and Spinal Cord

Page 2

Dkt: USF-001US

IN THE SPECIFICATION

Please amend the specification as follows:

Please amend the paragraph at the top of page 40 as follows:

Cord blood cells, cultured in the presence and absence of retinoic acid (RA) and Nerve Growth Factor (NGF), gave rise to cells bearing neural progenitor markers as evidenced by profiles of gene and protein expression. A total of 322 genes were either up- or down-regulated by a factor of at least 2, evidenced by measurements using a human microarray "gene chip." The greatest degree of up-regulation (44-fold increase) was seen in the mRNA for neurite outgrowth extension protein or pleiotrophin. A significant degree of ~~down-regulation~~ down-regulation was seen in the expression of tenascin (decreased 8.8 fold), an extracellular matrix protein that inhibits neurite outgrowth in developing neuronal ~~tissues~~ tissues, and in fibronectin (decreased 5.8 fold), an extracellular matrix protein that favors development of blood cell lineages. Other transcripts associated with neurogenesis that increased significantly (>2 fold) include glypican-4 (increased 4.9 fold), neuronal pentraxin II (increased 2.3 fold), neuronal growth associated protein 43 (increased 2.7 fold), and neuronal PAS1 (increased 2.3 fold). Musashi-1 was up-regulated 1.5 fold. A selection of other genes associated with neurogenesis that were up- or down-regulated is listed in Table I. Concomitant with the increased expression of markers indicative of neurogenesis (Table I), there was a decrease in expression of genes associated with hematopoiesis (Table II). The greatest changes occurred in the expression of HLA class I locus C heavy chain, macrophage receptor MARCO, secreted T cell activation protein Attractin (attractin), leucocyte immunoglobulin-like receptor-8 (LIR-8), thymocyte antigen CD1c, erythropoietin receptor and erythropoietin.

Please amend the bridging paragraph of pages 70-71 as follows:

Neurological and Motor Function Evaluation. Two days after TBI, significantly lower scores of Rotarod test and significantly higher scores of NSS in three groups compared to preinjury were found. Rotarod Test scores were significantly improved in TBI + HUCB group (138.0 [[-+]] \pm 11.3% and 155.2 [[-+]] \pm 16.2%) when compared with TBI (118.5 \pm 17.0% and 129.2 \pm 12.2%) and TBI + saline group (117.2 [[+-]] \pm 13.6% and 133.2 \pm 10.7%[[.]])($p < 0.05$) at days 14 and 28 ~~after~~ after administration of HUCB. The neurological-~~severity~~ severity scores were also significantly improved in TBI + HUCB group (4.2 [[+-]] \pm 1.3 and 3 \pm 0.8) when

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compared with TBI group (7.5 ± 1.73 and 6.3 ± 1.3) and TBI + saline group (7.3 ± 0.9 and 5.75 ± 0.9) [$[\cdot]$] ($p < 0.05$) at days 14 and 28 after the injection. The results indicate that intravenous administration of HUCB 24 hours after TBI ~~reduce~~ reduced the motor neurological functional deficits caused by TBI.